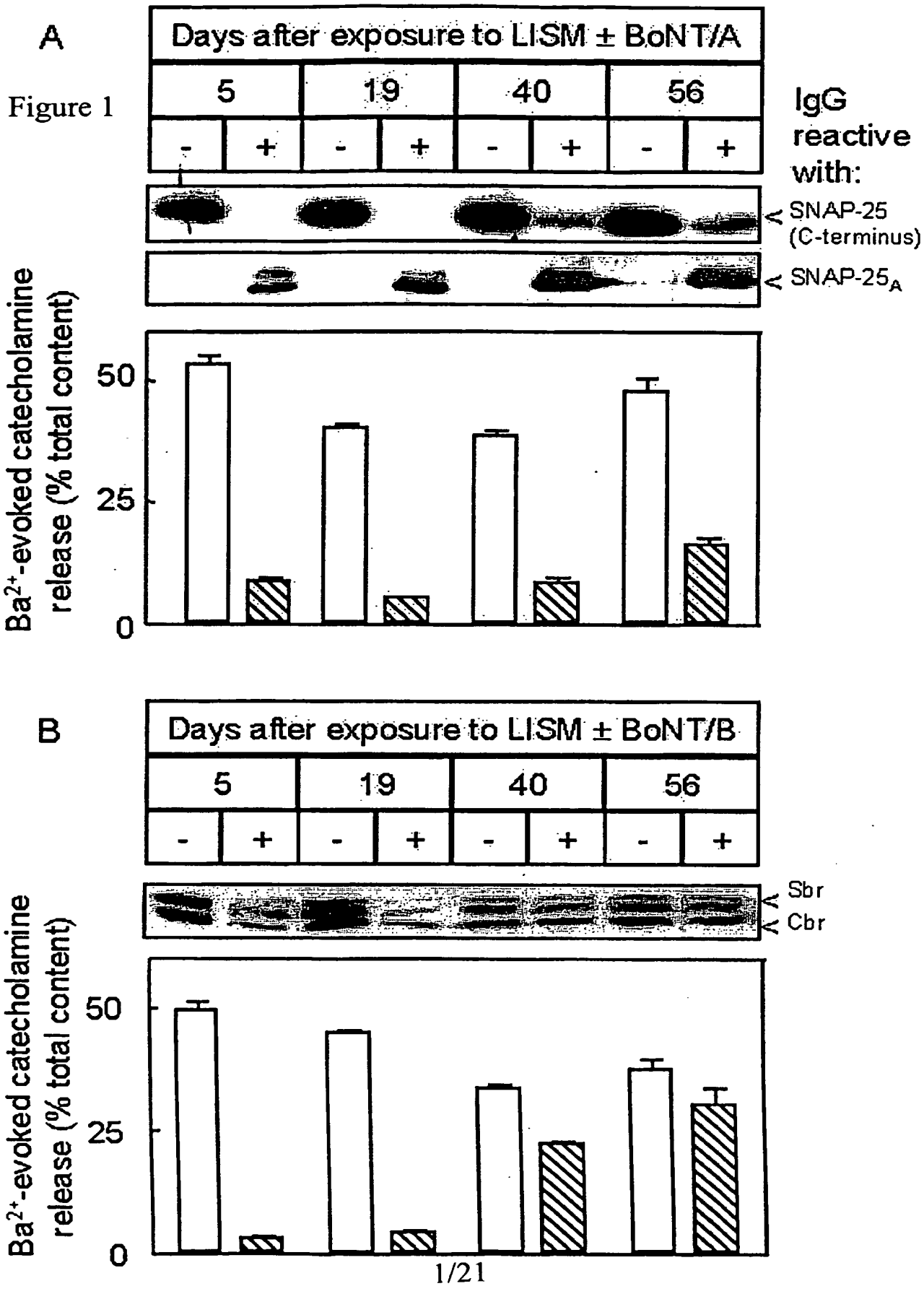
Figure 1



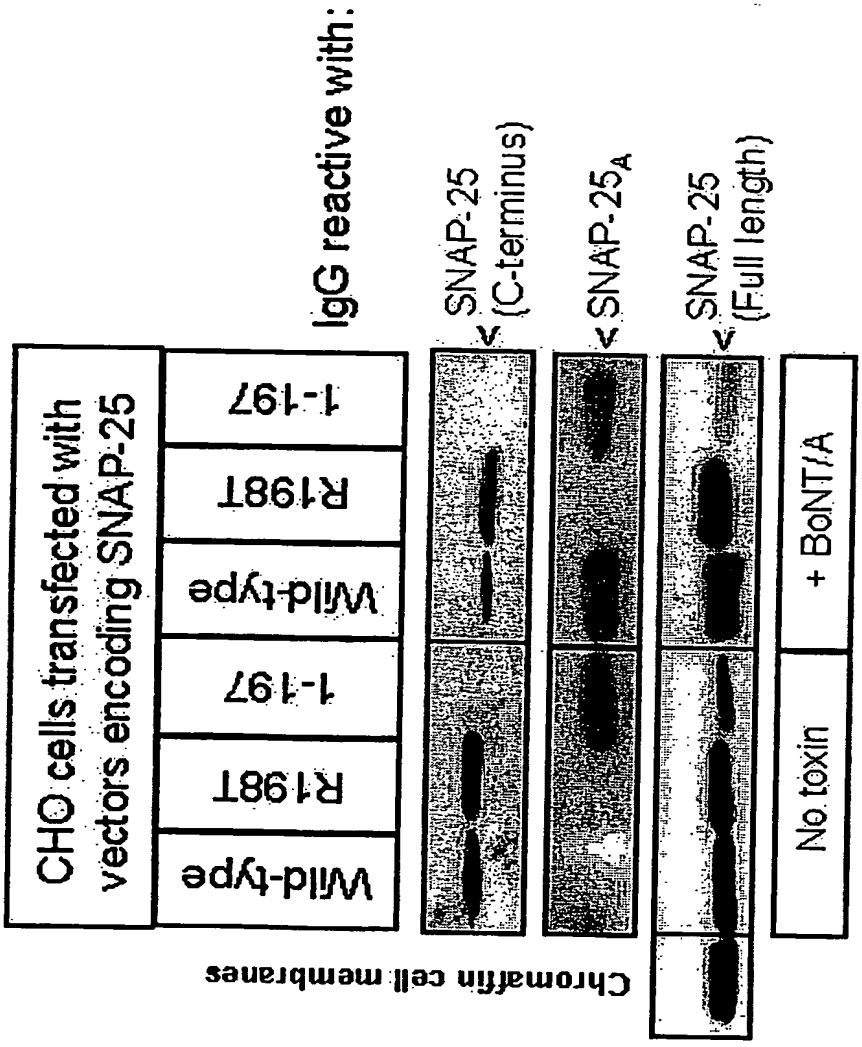


Figure 2 (page 1 of 2)

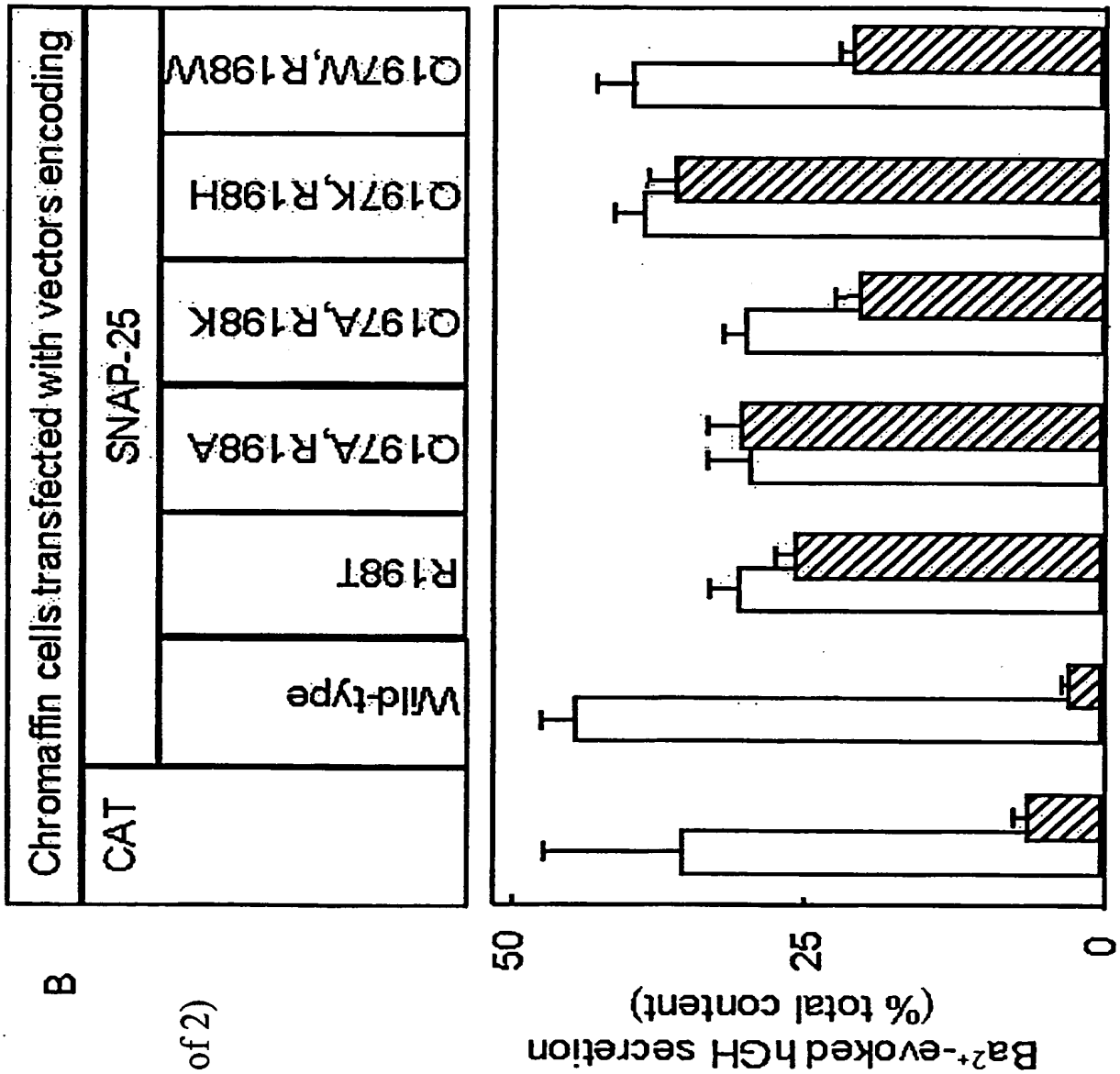
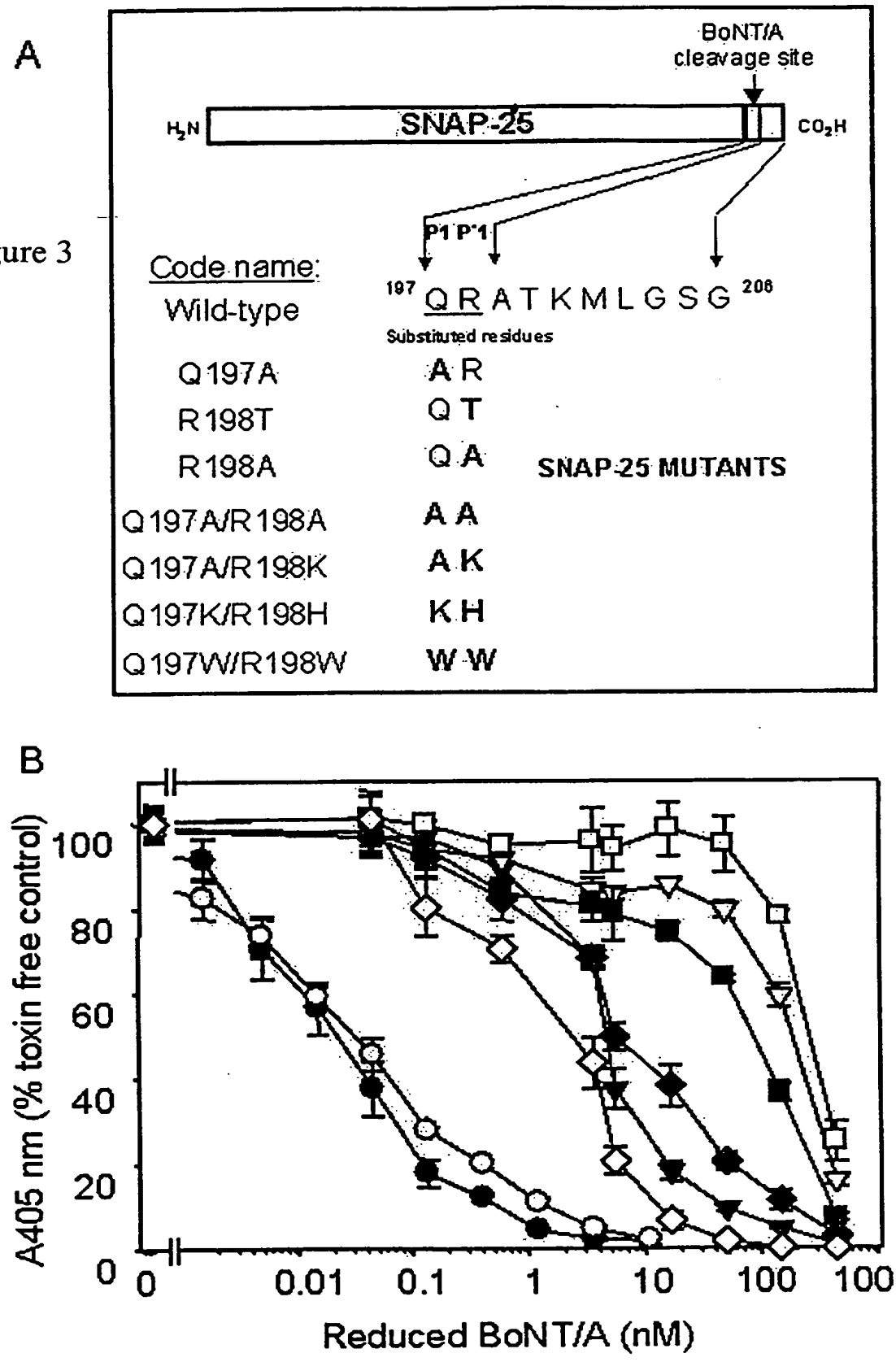


Figure 2 (page 2 of 2)

Figure 3



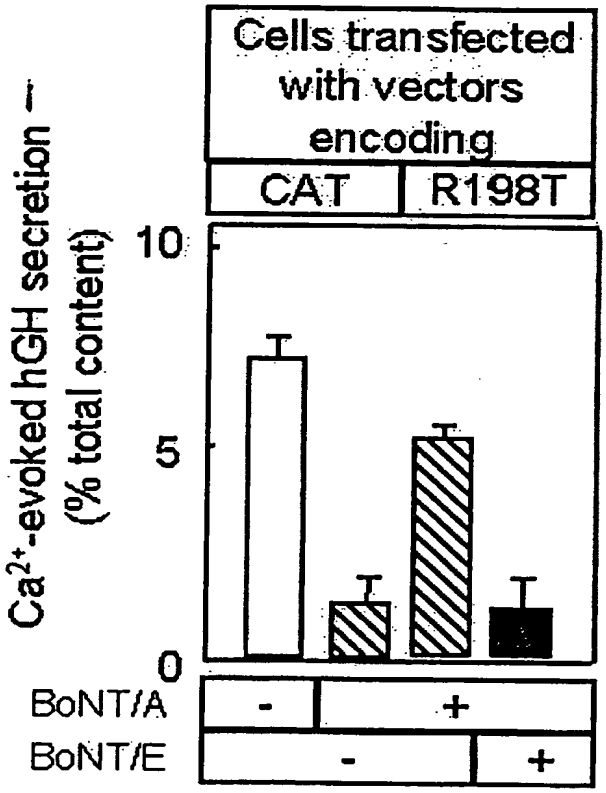

Cells transfected with vectors encoding
CAT
R198T
Ca2+-evoked hGH secretion – (% total content)
10
5
0
BoNT/A
-
+
BoNT/E
-
+

Figure 4

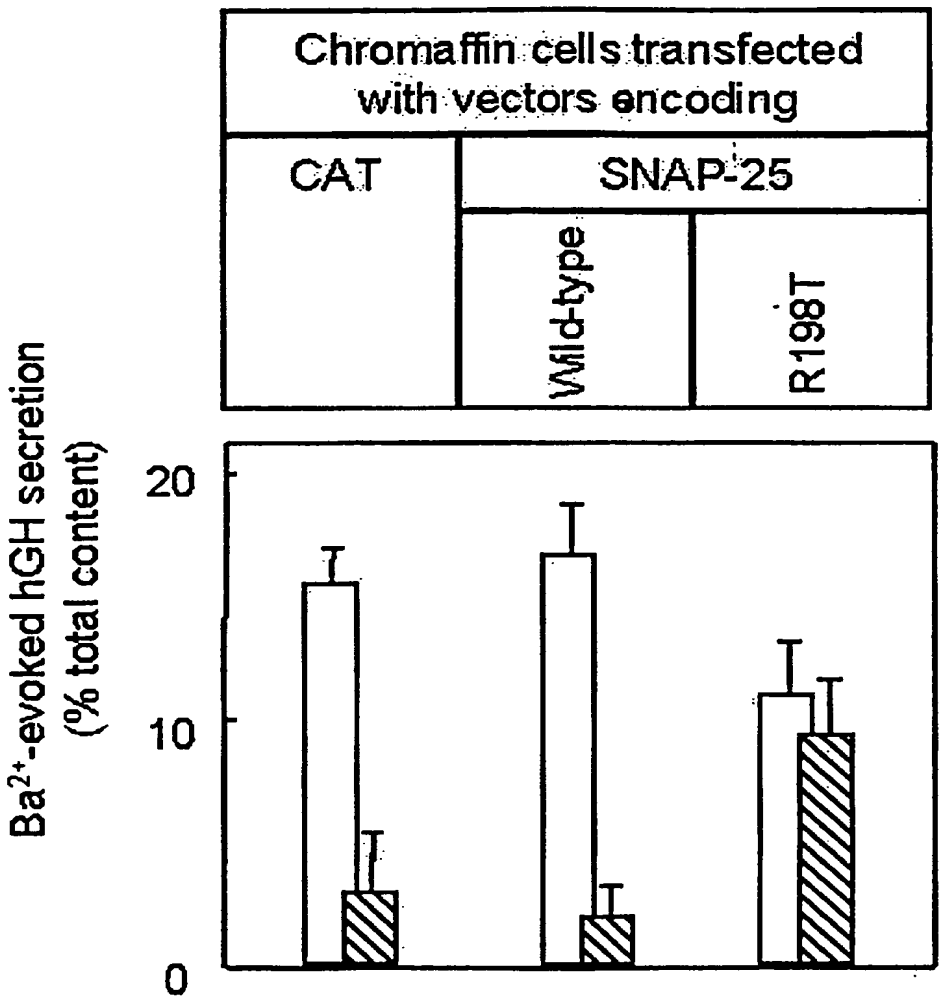

Chromaffin cells transfected with vectors encoding
CAT
SNAP-25
Wild-type
R198T
Ba2+-evoked hGH secretion (% total content)
20
10
0

Figure 5

A

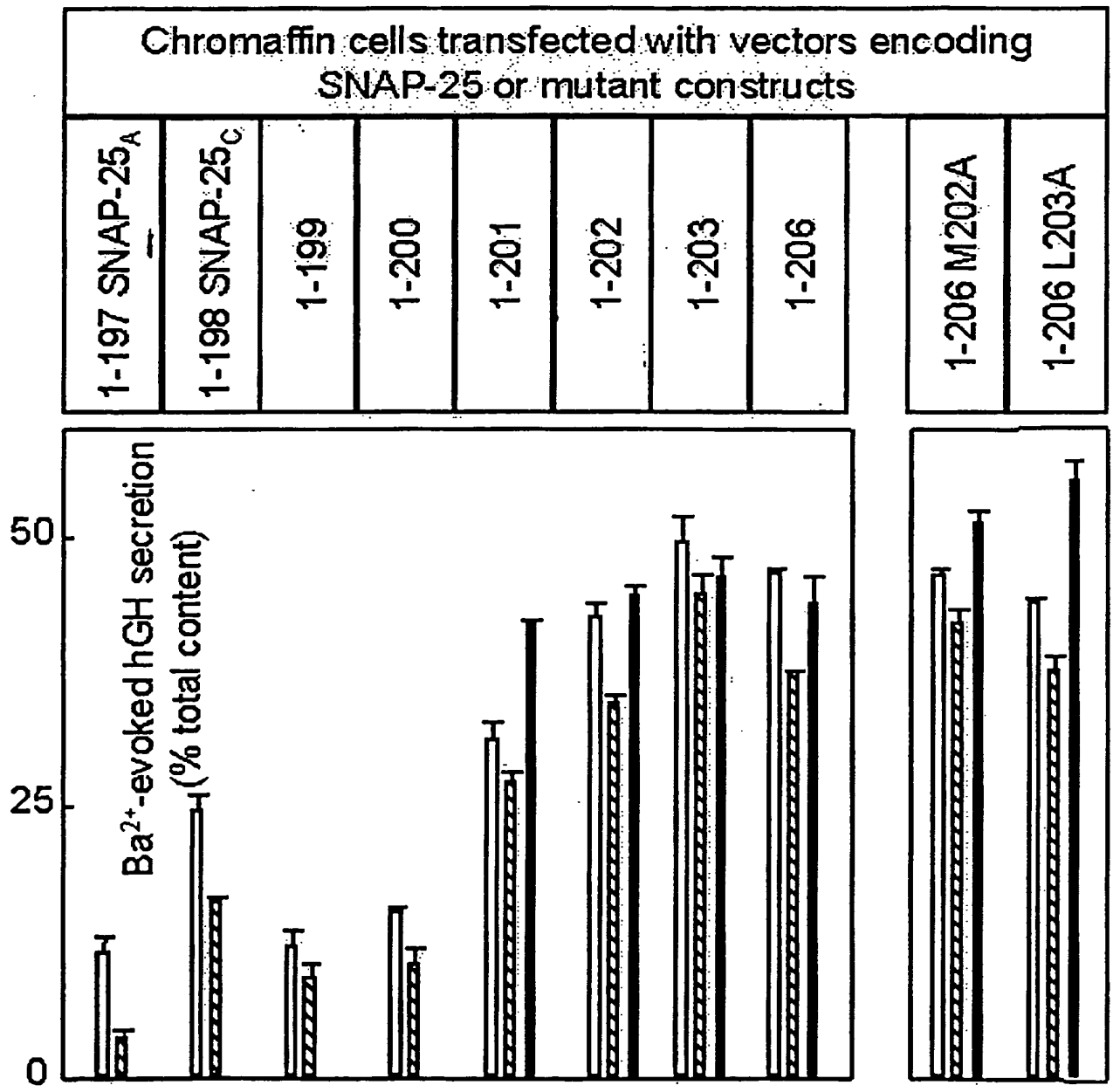


Figure 6 (page 1 of 2)

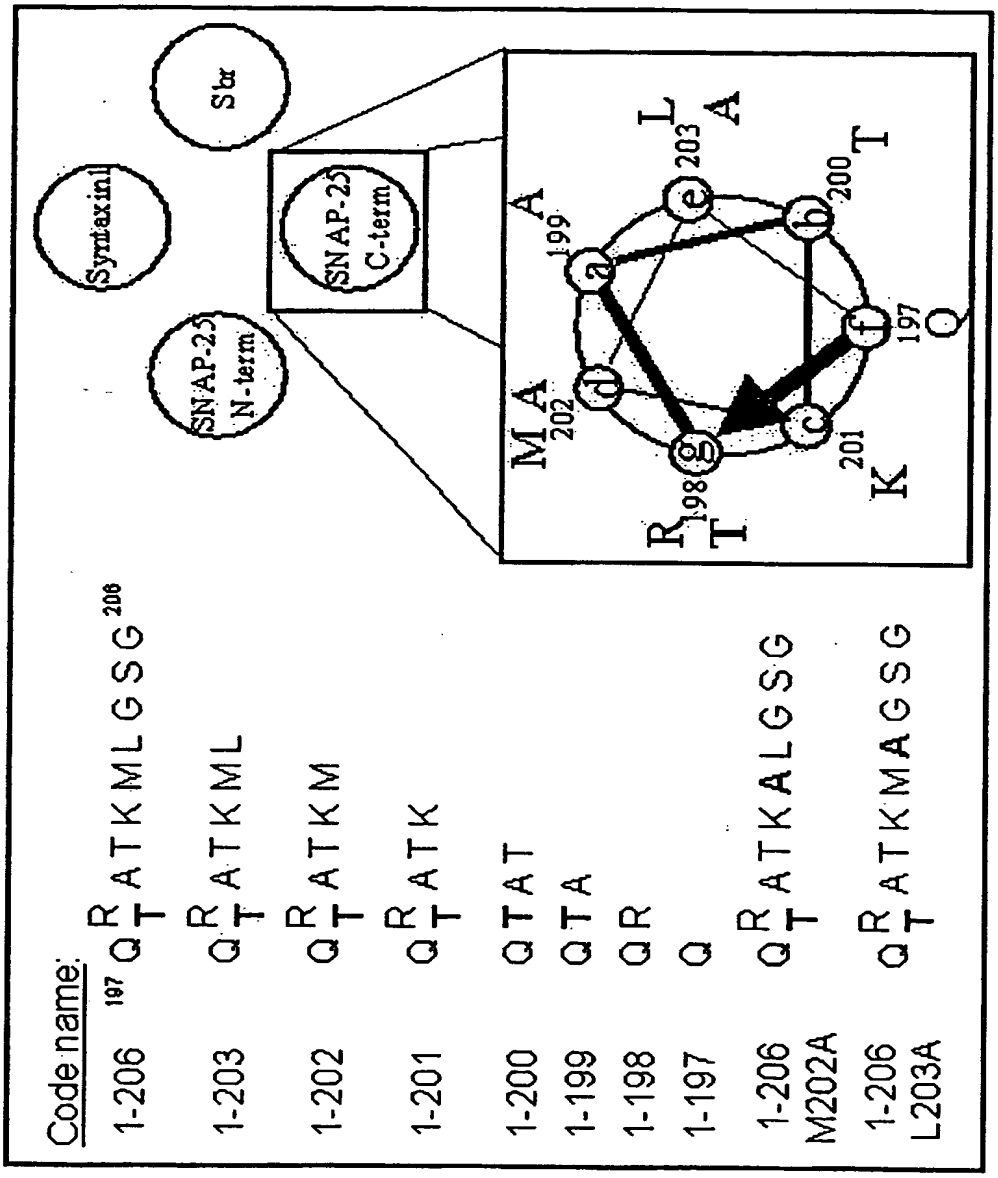


Figure 6 (page 2 of 2)

```
SNAP-25   145 - E M D E N L E Q V S G I I G N L R N M A L D M G N E I D T Q N R Q I
hSNAP-23  151 - E M E E N L T Q V G S I L G N L K D M A L N I G N E I D A Q N P Q I
mSNAP-23  150 - E M E E N L T Q V G S I L G N L K N M A L D M G N E I D A Q N Q Q I
                          :     : :           :       :           :     :

                      BoNT/E                          BoNT/A C
                        ⇓                               ⇓ ⇓
SNAP-25   179 - D [R I] M E K A D S N K T R I D E A N [Q R A] T K M L G S G - 206
hSNAP-23  185 - K R I T D K A D T N R D R I D I A N A R A K K L I D S   - 211
mSNAP-23  184 - Q [K I] T E K A D T N K N R I D I A N [T R] A K K L I D S   - 210
                    :     :           :     :     :     :       :
```

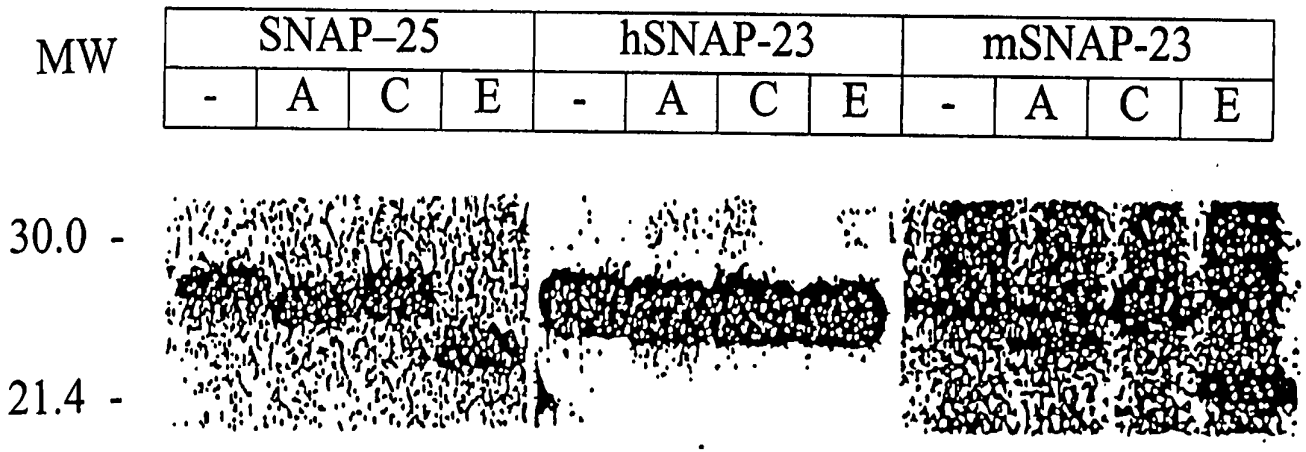



Figure 7

```
LOCUS HSVAMP1MR 354 bp mRNA PRI 17-FEB-1997
DEFINITION H.sapiens Vamp1 mRNA.
ACCESSION Z48924 VERSION Z48924.1 GI:758107

protein_id="CAA88760.1" /db_xref="GI:758108"
/db_xref="SWISS-PROT:P23763"
/translation="MSAPAQPPAEGTEGTAPGGGPPGPPPNMTSNRRLQQT
QAQVEEVVDIIRVNVDKVLERDQKLSELDDRADALQAGASQFESSAAKLKR
KYWWKNCKMMIMLG TICAIIVVVIVIYFFT"
BASE COUNT 96 a 82 c 103 g 73 t
ORIGIN
1 atgtctgctc cagctcagcc acctgctgaa gggacagaag
ggactgcccc aggtgggggt
61 ccccctggcc ctcctcctaa catgaccagt aacagacgac
tgcagcaaac ccaggcacaa
121 gtggaggagg tggtggacat catacgtgtg aacgtggaca
aggtcctgga gagggaccag
181 aagctgtcag agctggatga ccgagctgat gccttgcagg
caggagcatc acaatttgag
241 agcagtgctg caaagctaaa gaggaagtat tggtggaaaa
actgcaagat gatgatcatg
301 ctgggaacca tctgtgccat catcgtggta gttattgtaa
tctacttttt tact //
```

Figure 8 (page 1 of 11)

GenBank Acc: AI815549 GenBank gi: 5431095
IMAGE:2517969 (5')

GAGCCGCCGCCGCCATCACTGCCGCTGCCAAGTCCTCCACCCGCTGCCCCC
GCCATGTCTGCTACCGCTGCCACGGCCCCCCCTGCTGCCCCGGCTGGGGAG
GGTGGTCCCCCTGCACCCCCTCCAAACCTCACCAGTAACAGGAGACTGCAG
CAGACCCAGGCCCAGGTGGATGAGGTGGTGGACATCATGAGGGTGAACGTG
GACAAGGTCCTGGAGCGAGACCAGAAGCTGTCGGAGCTGGACGACCGTGCA
GATGCACTCCAGGCGGGGGCCTCCCAGTTTGAAACAAGCGCAGCCAAGCTC
AAGCGCAAATACTGGTGGAAAAACCTCAAGATGATGATCATCTTGGGAGTG
ATTTGCGCCATCATCCTCATCATCATCATAGTTTACTTCAGCACTTAAATC
CCCGAGGAGTCTGCCCTGCCTAGAGAAGGGCCTCTCCCCCAACCCTCAGCC
GTTCCTCCACCTCTCAGCCAT ATCTNTCAGCCCCCCCTC

Figure 8 (page 2 of 11)

EST name: ui73f02.y1 GenBank Acc: AI785090 GenBank gi: 5332806 Clone Id: IMAGE:1888059 (5')

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ACCCCCGCCATGTCGGCTACCGCTGCCACCGTCCCGCCTGCCGCCCCGGCC
GGCGAGGGTGGCCCCCCTGCACCTCCTCCAAACCTTACTAGTAACAGGAGA
CTGCAGCAGACCCAGGCCCAGGTGGATGAGGTGAGTGTGTGTGTGTCTG
TGTCTGTGTCTATGTCTATGTATGTCAAAGATGCAAGATGATGGGCTGGCA
AATAGGTGTGGGAGCCCATCTTGGGTTGAAGGTAAAGACAGCTTATGCTTG
TGGGTTTTGGTCGGAGACCTGCCTCAT

Figure 8 (page 3 of 11)

```
LOCUS NM_004781 638 bp mRNA PRI 27-JUN-2000
DEFINITION Homo sapiens vesicle-associated membrane
protein 3 (cellubrevin) (VAMP3), mRNA.
ACCESSION NM_004781 VERSION NM_004781.2 GI:9257252
   protein_id="NP_004772.1" /db_xref="GI:4759300"
/translation="MSTGPTAATGSNRRLQQTQNQVDEVVDIMRVNVDKVL
ERDQKLS
ELDDRADALQAGASQFETSAAKLKRKYWWKNCKMWAIGITVLVIFIIIIV
WVVSS" BASE COUNT 181 a 133 c 141 g 183 t ORIGIN 1
ctctaaagcg ccgcagctgc caaaatgtct acaggtccaa
ctgctgccac tggcagtaat 61 cgaagacttc agcagacaca
aaatcaagta gatgaggtgg tggacataat gcgagttaac 121
gtggacaagg ttctggaaag agaccagaag ctctctgagt
tagacgaccg tgcagacgca 181 ctgcaggcag gcgcttctca
atttgaaacg agcgcagcca agttgaagag gaaatattgg 241
tggaagaatt gcaagatgtg ggcaatcggg attactgttc
tggttatctt catcatcatc 301 atcatcgtgt gggttgtctc
ttcatgaaga accagcggaa ctcaaaactg ctgttcaaga 361
aacctcttca agacttttga cttagaacct gctatattat
caagcttacc tactgttatc 421 tctaaaattt tttttgtgtt
aatgtaaagt tgaatttcta ggaaacgtgc ctttgttttt 481
taatatgcac tccaaattag aaggccggcc ccgtccacat
tttgcacagt gcctttacag 541 atttacgtat gggctgatga
agaggccttc ttaagttcca gagtgctata atctagatgt 601
aatgttgtca ctaattaatt gccattactc ccctttag //
```

Figure 8 (page 4 of 11)

LOCUS HSU55936 800 bp mRNA PRI 14-JUN-1996
DEFINITION Human SNAP-23 mRNA, complete cds.
ACCESSION U55936 VERSION U55936.1 GI:1374812
SOURCE human.

protein_id="AAC50537.1" /db_xref="GI:1374813"

/translation="MDNLSSEEIQQRAHQITDESLESTRRILGLAIESQDA
GIKTITMLDEQKEQLNRIEEGLDQINKDMRETEKTLTELNKCCGLCVCPCN
RTKNFESGKAYKTTWGDGGENSPCNVVSKQPGPVTNGQLQQPTTGAVSGGY
IKRITNDAREDEMEENLTQVGSILGNLKDMALNIGNEIDAQNPQIKRITDK
ADTNRDRIDIANARAKKLIDS"
BASE COUNT 266 a 167 c 192 g 175 t ORIGIN
1 ctcgaggcca cgaaggccgc caggtccggt gttggggtgt
ccgagttgcc gccggagagg 61 agtggcctcg cccgcttgag
ttttgattca tcatggataa tctgtcatca gaagaaattc 121
aacagagagc tcaccagatt actgatgagt ctctggaaag
tacgaggaga atcctgggtt 181 tagccattga gtctcaggat
gcaggaatca agaccatcac tatgctggat gaacaaaagg 241
aacaactaaa ccgcatagaa gaaggcttgg accaaataaa
taaggacatg agagagacag 301 agaagacttt aacagaactc
aacaaatgct gtggcctttg tgtctgccca tgtaatagaa 361
caaagaactt tgagtctggc aaggcttata agacaacatg
gggagatggt ggagaaaact 421 caccttgcaa tgtagtatct
aaacagccag gcccggtgac aaatggtcag cttcagcaac 481
caacaacagg agcagtcagt ggtggataca ttaaacgcat
aactaatgat gccagagaag 541 atgaaatgga agagaacctg
actcaagtgg gcagtatcct gggaaatcta aaagacatgg 601
ccctgaacat aggcaatgag attgatgctc aaaatccaca
aataaaacga atcacagaca 661 aggctgacac caacagagat
cgtattgata ttgccaatgc cagagcaaag aaactcattg 721
acagctaaag ctactgctgt tcttctttat catttattca
cttccgtagc tcctccttga 781 aagttattac cttttcagag

Figure 8 (page 5 of 11)

```
DEFINITION  Human nerve-terminal protein (isoform
SNAP25A) mRNA, complete cds.
ACCESSION   L19760
VERSION     L19760.1  GI:307425
SOURCE      Homo sapiens cDNA to mRNA.

/protein_id="AAC37545.1"
/db_xref="GI:307426"

/translation="MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVE
ESKDAGIRTLVMLDEQGEQLDRVEEGMNHINQDMKEAEKNLKDLGKCCGLF
ICPCNKLKSSDAYKKAWGNNQDGVVASQPARVVDEREQMAISGGFIRRVTN
DARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDRIMEKADSNKT
RIDEANQRATKMLGSG"

BASE COUNT      260 a    223 c    237 g    203 t
ORIGIN
1 aacacaaccc tcccgagaag cccaggtcca gagccaaacc
cgtcactgac cccccagccc
61 aggcgcccag ccactcccca ccgctaccat ggccgaagac
gcagacatgc gcaatgagct
121 ggaggagatg cagcgaaggg ctgaccagtt ggctgatgag
tcgctggaaa gcacccgtcg
181 tatgctgcaa ctggttgaag agagtaaaga tgctggtatc
aggactttgg ttatgttgga
241 tgaacaagga gaacaactcg atcgtgtcga agaaggcatg
aaccatatca accaagacat
301 gaaggaggct gagaaaaatt taaaagattt agggaaatgc
tgtggccttt tcatatgtcc
361 ttgtaacaag cttaaatcaa gtgatgctta caaaaaagcc
tggggcaata atcaggatgg
421 agtggtggcc agccagcctg ctcgtgtagt ggacgaacgg
gagcagatgg ccatcagtgg
481 cggcttcatc cgcagggtaa caaatgatgc ccgagaaaat
gaaatggatg aaaacctaga
541 gcaggtgagc ggcatcatcg ggaacctccg tcacatggcc
ctggatatgg gcaatgagat
601 cgatacacag aatcgccaga tcgacaggat catggagaag
gctgattcca acaaaaccag
```

Figure 8 (page 6 of 11)

```
661 aattgatgag gccaaccaac gtgcaacaaa gatgctggga
agtggttaag tgtgcccacc
721 cgtgttctcc tccaaatgct gtcgggcaag atagctcctt
catgcttttc tcatggtatt
781 atctagtagg tctgcacaca taacacacat cagtccaccc
ccattgtgaa tgttgtcctg
841 tgtcatctgt cagcttccca acaatacttt gtgtcttttg
ttctctcttg gtctctttct
901 ttccaaaggt tgtacatagt ggt
//
```

Figure 8 (page 7 of 11)

LOCUS HUMSNAP25B 923 bp mRNA PRI 25-MAR-1994
DEFINITION Human nerve-terminal protein (isoform SNAP-25b) mRNA, complete cds.
ACCESSION L19761 VERSION L19761.1 GI:307427

/protein_id="AAC37546.1" /db_xref="GI:307428"
/translation="MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVE
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VCPCNKLKSSDAYKKAWGNNQDGVVASQPARVVDEREQMAISGGFIRRVTN
DARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDRIMEKADSNKT
RIDEANQRATKMLGSG"
BASE COUNT 260 a 223 c 243 g 197 t ORIGIN
1 aacacaaccc tcccgagaag cccaggtcca gagccaaacc
cgtcactgac cccccagccc 61 aggcgcccag ccactcccca
ccgctaccat ggcccaagac gcagacatgc gcaatgagct 121
ggaggagatg cagcgaaggg ctgaccagtt ggctgatgag
tcgctggaaa gcacccgtcg 181 tatgctgcaa ctggttgaag
agagtaaaga tgctggtatc aggactttgg ttatgttgga 241
tgaacaagga gaacaactgg aacgcattga ggaagggatg
gaccaaatca ataaggacat 301 gaaagaagca gaaaagaatt
tgacggacct aggaaaattc tgcgggcttt gtgtgtgtcc 361
ctgtaacaag cttaaatcaa gtgatgctta caaaaaagcc
tggggcaata atcaggacgg 421 agtggtggcc agccagcctg
ctcgtgtagt ggacgaacgg gagcagatgg ccatcagtgg 481
cggcttcatc cgcagggtaa caaatgatgc ccgagaaaat
gaaatggatg aaaacctaga 541 gcaggtgagc ggcatcatcg
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cgatacacag aatcgccaga tcgacaggat catggagaag
gctgattcca acaaaaccag 661 aattgatgag gccaaccaac
gtgcaacaaa gatgctggga agtggttaag tgtgcccacc 721
cgtgttctcc tccaaatgct gtcgggcaag atagctcctt
catgcttttc tcatggtatt 781 atctagtagg tctgcacaca
taacacacat cagtccaccc ccattgtgaa tgttgtcctg 841
tgtcatctgt cagcttccca acaatacttt gtgtcttttg
ttctctcttg gtctctttct 901 ttccaaaggt tgtacatagt ggt

Figure 8 (page 8 of 11)

LOCUS HUMSYN1A 2088 bp mRNA PRI 28-NOV-1994
DEFINITION Human syntaxin 1A mRNA, complete cds.
ACCESSION L37792 VERSION L37792.1 GI:577487
Swiss-Prot Accession Number P32851
protein_id="AAA53519.1" /db_xref="GI:577488"
/translation="MKDRTQELRTAKDSDDDDVAVTVDRDRFMDEFFEQV
EEIRGFIDKIAENVEEVKRKHSAILASPNPDEKTKEELEELMSDIKKTANK
VRSKLKSIEQSIEQEEGLNRSSADLRIRKTQHSTLSRKFVEVMSEYNATQS
DYRERCKGRIQRQLEITGRTTTSEELEDMLESGNPAIFASGIIMDSSISKQ
ALSEIETRHSEIIKLENSIRELHDMFMDMAMLVESQGEMIDRIEYNVEHAV
DYVERAVSDTKKAVKYQSKARRKKIMIIICCVILGIVIASTVGGIFA"

BASE COUNT 447 a 635 c 604 g 402 t ORIGIN
1 catgaaggac cgaacccagg agctccgcac ggccaaggac
agcgatgatg atgatgatgt 61 cgctgtcacc gtggaccgag
accgcttcat ggatgagttc tttgagcagg tggaggagat 121
tcgaggcttc attgacaaga tcgcagagaa cgtggaggag
gtgaagcgga agcacagtgc 181 catcctggca tcccccaacc
ccgatgagaa gacgaaggag gagctggaag aactcatgtc 241
cgacataaag aagacagcaa acaaagttcg ttccaagtta
aagagcatcg agcagtccat 301 cgagcaagag gaaggcctga
accgctcctc cgctgacctg aggatccgga agacacagca 361
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tacaacgcca cgcagtccga 421 ctaccgcgag cgctgcaaag
gccgcatcca gaggcagctg gagatcaccg gcaggaccac 481
gaccagtgag gagctggagg acatgctgga gagtgggaac
cccgccatct ttgcctctgg 541 gatcatcatg gactccagca
tctcgaagca ggctctgagc gagattgaga cgcggcacag 601
tgagatcatc aagctggaga acagcatccg tgagctacac
gacatgttca tggacatggc 661 catgctcgtg gagagccagg
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ggtagactat gtggagaggg ccgtgtctga caccaagaag
gccgtcaagt accagagcaa 781 ggcgcgccgg aagaaaatca
tgatcatcat ctgctgtgtg atcctgggca tcgtcatcgc 841
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tgcatgatct ctgtgagtgt gcgtctgtac gggaagaggc 1081

Figure 8 (page 9 of 11)

```
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ccacgcttcc ttgccttcag taactcggtg ggcccaggtt 1201
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ctgccctgtc ctctccagct 1261 gtccccacaa gcagagccct
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ccttgtggac aggcagggag 1861 atgcatgcga gtgcatgcag
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gctttactcc tgcccagtga ctgtgaccac tgtccgtgtt
gccttcttga acagcgattc 1981 cccccaaccc cttcaccaaa
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tgtagaataa acatttgtat ctgtaaaaaa aaaaaaaaaa
aagcgttc //
```

Figure 8 (page 10 of 11)

```
                    10        20        30        40        50
HUMANS25.PRO MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVML
             ||||||||||||||||||||||||||||||||||||||||||||||||||
MOUSES25.PRO MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVML
                    10        20        30        40        50

                    60        70        80        90       100
HUMANS25.PRO DEQGEQLDRVEEGMNHINQDMKEAEKNLKDLGKCCGLFICPCNKLKSSDA
             |||||||:|:||||::||:||||||||.|||| ||| :||||||||||
MOUSES25.PRO DEQGEQLERIEEGMDQINKDMKEAEKNLTDLGKFCFLCVCPCNKLKSSDA
                    60        70        80        90       100

                   110       120       130       140       150
HUMANS25.PRO YKKAWGNNQDGVVASQPARVVDEREQMAISGGFIRRVTNDARENEMDENL
             ||||||||||||||||||||||||||||||||||||||||||||||||||
MOUSES25.PRO YKKAWGNNQDGVVASQPARVVDEREQMAISGGFIRRVTNDARENEMDENL
                   110       120       130       140       150

                   160       170       180       190       200
HUMANS25.PRO EQVSGIIGNLRHMALDMGNEIDTQNRQIDRIMEKADSNKTRIDEANQRAT
             ||||||||||||||||||||||||||||||||||||||||||||||||||
MOUSES25.PRO EQVSGIIGNLRHMALDMGNEIDTQNRQIDRIMEKADSNKTRIDEANQRAT
                   160       170       180       190       200

HUMANS25.PRO KMLGSG
             ||||||
MOUSES25.PRO KMLGSG

Lipman-Pearson Protein Alignment
Ktuple: 2; Gap Penalty: 4; Gap Length Penalty: 12
Seq1(1>206) HUMANS25.PRO
Seq2(1>206) MOUSES25.PRO
Similarity Index 95.6 Gap Number 0 Gap Length 0
Consensus Length 206
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Figure 8 (page 11 of 11)

Figure 9